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=> d his

     (FILE 'HOME' ENTERED AT 16:29:01 ON 10 JAN 2003)

     FILE 'MEDLINE, CAPLUS, BIOSIS, SCISEARCH' ENTERED AT 16:29:29 ON 10 JAN
     2003
L1          5018 S AROMATIC(3A)AMINO(3A)ACID(3A)DECARBOXYLASE OR AADC
L2         89286 S PARKINSON(4A)DISEASE
L3           465 S L1 AND L2
L4           246 S L1(S)L2
L5        397803 S CENTRAL(W)NERVOUS(W)SYSTEM OR CNS
L6            26 S L4 AND L5
L7          2942 S AROMATIC(W)AMINO(W)ACID(W)DECARBOXYLASE OR AADC
L8          2942 S L1(S)L7
L9           180 S L2(S)L7
L10           21 S L5 AND L9
L11           10 DUP REM L10 (11 DUPLICATES REMOVED)
L12           14 DUP REM L6 (12 DUPLICATES REMOVED)

=> d au ti so 1-14 l12

L12  ANSWER 1 OF 14  CAPLUS  COPYRIGHT 2003 ACS
IN   Ozawa, Keiya; Fujimoto, Ken-ichi; Muramatsu, Shin-ichi; Ikeguchi,
     Kunihiko; Nakano, Imaharu
TI   Methods of treating Parkinson's disease using recombinant adeno-associated
     virus virions
SO   U.S. Pat. Appl. Publ., 10 pp.
     CODEN: USXXCO

L12  ANSWER 2 OF 14  CAPLUS  COPYRIGHT 2003 ACS
IN   Kaplitt, Michael G.; During, Matthew J.
TI   AAV-mediated delivery of DNA to cells of the nervous system
SO   U.S., 23 pp., Cont.-in-part of U.S. Ser. No. 227,319, abandoned.
     CODEN: USXXAM

L12  ANSWER 3 OF 14  BIOSIS  COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AU   Azzouz, M. (1); Martin-Rendon, E. (1); Rohll, J. B. (1); Ellard, F. M.
     (1); Olsen, A. (1); Carter, E. E. (1); Mitrophanous, K. A. (1); Kingsman,
     S. M. (1); Mazarakis, N. D. (1)
TI   Gene transfer to the nervous system using Equine Infectious Anaemia Virus
     based lentiviral vectors.
SO   Society for Neuroscience Abstracts, (2001) Vol. 27, No. 1, pp. 526. print.
     Meeting Info.: 31st Annual Meeting of the Society for Neuroscience San
     Diego, California, USA November 10-15, 2001
     ISSN: 0190-5295.

L12  ANSWER 4 OF 14     MEDLINE
AU   Kang U J; Lee W Y; Chang J W
TI   Gene therapy for Parkinson's disease: determining the genes necessary for
     optimal dopamine replacement in rat models.
SO   HUMAN CELL, (2001 Mar) 14 (1) 39-48.  Ref: 54
     Journal code: 8912329. ISSN: 0914-7470.

L12  ANSWER 5 OF 14     MEDLINE                              DUPLICATE 1
AU   Bankiewicz K S; Eberling J L; Kohutnicka M; Jagust W; Pivirotto P; Bringas
     J; Cunningham J; Budinger T F; Harvey-White J
TI   Convection-enhanced delivery of AAV vector in parkinsonian monkeys; in
     vivo detection of gene expression and restoration of dopaminergic function
     using pro-drug approach.
SO   EXPERIMENTAL NEUROLOGY, (2000 Jul) 164 (1) 2-14.
     Journal code: 0370712. ISSN: 0014-4886.

L12  ANSWER 6 OF 14  BIOSIS  COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
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AU Lee, M. A. (1); Lee, H. S.; Jung, S. H.; Park, S. Y.; Huh, S. O.; Ryu, J. K.; Kim, H. J.; Jin, B. K.; Ichinose, H.; Kim, S. U.
TI Human neural stem cells transfected with Nurr1 gene express dopaminergic phenotype.
SO Society for Neuroscience Abstracts, (2000) Vol. 26, No. 1-2, pp. Abstract No.-313.7. print.
Meeting Info.: 30th Annual Meeting of the Society of Neuroscience New Orleans, LA, USA November 04-09, 2000 Society for Neuroscience . ISSN: 0190-5295.

L12 ANSWER 7 OF 14 CAPLUS COPYRIGHT 2003 ACS
IN Bankiewicz, Krys; Cunningham, Janet; Eberling, Jamie L.
TI Convection-enhanced delivery of AAV vectors to the **CNS** and therapeutic use thereof
SO PCT Int. Appl., 74 pp.
CODEN: PIXXD2

L12 ANSWER 8 OF 14 MEDLINE DUPLICATE 2
AU Imaoka T; Date I; Ohmoto T; Nagatsu T
TI Significant behavioral recovery in Parkinson's disease model by direct intracerebral gene transfer using continuous injection of a plasmid DNA-liposome complex.
SO HUMAN GENE THERAPY, (1998 May 1) 9 (7) 1093-102.
Journal code: 9008950. ISSN: 1043-0342.

L12 ANSWER 9 OF 14 MEDLINE DUPLICATE 3
AU Moffat M; Harmon S; Haycock J; O'Malley K L
TI L-Dopa and dopamine-producing gene cassettes for gene therapy approaches to Parkinson's disease.
SO EXPERIMENTAL NEUROLOGY, (1997 Mar) 144 (1) 69-73.
Journal code: 0370712. ISSN: 0014-4886.

L12 ANSWER 10 OF 14 MEDLINE DUPLICATE 4
AU Opacka-Juffry J; Brooks D J
TI L-dihydroxyphenylalanine and its decarboxylase: new ideas on their neuroregulatory roles.
SO MOVEMENT DISORDERS, (1995 May) 10 (3) 241-9. Ref: 54
Journal code: 8610688. ISSN: 0885-3185.

L12 ANSWER 11 OF 14 SCISEARCH COPYRIGHT 2003 ISI (R)
AU NEFF N H (Reprint); HADJICONSTANTINOU M
TI **AROMATIC** L-**AMINO-ACID DECARBOXYLASE** MODULATION AND **PARKINSONS-DISEASE**
SO PROGRESS IN BRAIN RESEARCH, (1995) Vol. 106, pp. 91-97.
ISSN: 0079-6123.

L12 ANSWER 12 OF 14 MEDLINE DUPLICATE 5
AU Misu Y; Goshima Y
TI Is L-dopa an endogenous neurotransmitter?.
SO TRENDS IN PHARMACOLOGICAL SCIENCES, (1993 Apr) 14 (4) 119-23. Ref: 31
Journal code: 7906158. ISSN: 0165-6147.

L12 ANSWER 13 OF 14 MEDLINE DUPLICATE 6
AU Nishi K; Kondo T; Narabayashi H
TI A mouse model of N-methyl-4-phenyl-1,2,3,6-tetrahydropyridine induced parkinsonism: effect of norepinephrine terminal destruction.
SO NO TO SHINKEI. BRAIN AND NERVE, (1987 Jul) 39 (7) 663-72. Ref: 34
Journal code: 0413550. ISSN: 0006-8969.

L12 ANSWER 14 OF 14 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AU MAGNUSSEN I; RAND J H; VAN WOERT M H; JENSEN T S
TI PLASMA ACCUMULATION AND METABOLISM OF ORALLY ADMINISTERED SINGLE DOSE L-5 HYDROXY TRYPTOPHAN IN MAN.
SO ACTA PHARMACOL TOXICOL, (1981) 49 (3), 184-189.

CODEN: APTOA6. ISSN: 0001-6683.

=> d bib ab 1-14 l12

L12 ANSWER 1 OF 14 CAPLUS COPYRIGHT 2003 ACS
AN 2002:889382 CAPLUS
DN 137:363095
TI Methods of treating Parkinson's disease using recombinant adeno-associated virus virions
IN Ozawa, Keiya; Fujimoto, Ken-ichi; Muramatsu, Shin-ichi; Ikeguchi, Kunihiko; Nakano, Imaharu
PA Japan
SO U.S. Pat. Appl. Publ., 10 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2002172664	A1	20021121	US 2002-96723	20020313
PRAI US 2001-275903P	P	20010314		

AB Methods for treating Parkinson's disease (PD) are provided. Recombinant adeno-assocd. virus (rAAV) virions are used to deliver genes encoding dopamine-synthesizing enzymes to the **central nervous system** of a primate. Once delivered, the genes are expressed, which then results in dopamine synthesis and amelioration in the clin. signs and symptoms of PD. The methods of the present invention can be used to deliver the three central dopamine synthesizing enzymes: tyrosine hydroxylase, arom. L-amino acid decarboxylase, and guanosine triphosphate cyclohydrolase I thereby enhancing dopamine biosynthesis and providing for enhanced therapeutic efficacy.

L12 ANSWER 2 OF 14 CAPLUS COPYRIGHT 2003 ACS
AN 2001:75298 CAPLUS
DN 134:126803
TI AAV-mediated delivery of DNA to cells of the nervous system
IN Kaplitt, Michael G.; During, Matthew J.
PA The Rockefeller University, USA; Yale University
SO U.S., 23 pp., Cont.-in-part of U.S. Ser. No. 227,319, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 6180613	B1	20010130	US 1995-467044	19950606
CA 2187626	AA	19951026	CA 1995-2187626	19950413
US 6503888	B1	20030107	US 2000-548176	20000413
PRAI US 1994-227319	B2	19940413		
US 1995-467044	A1	19950606		

AB The invention relates to a method of delivering exogenous DNA to a target cell of the mammalian **central nervous system** using an adeno-assocd. virus (AAV)-derived vector. Also included in the invention are the AAV-derived vectors contg. exogenous DNA which encodes a protein or proteins which treat nervous system disease, and a method of treating such disease. The invention relates to a method of delivering exogenous DNA to a target cell of the mammalian **central nervous system** using an adeno-assocd. virus (AAV)-derived vector. Also included in the invention are the AAV-derived vectors contg. exogenous DNA which encodes a protein or proteins which prevent or treat nervous system disease, and a method of preventing or treating such disease.
RE.CNT 68 THERE ARE 68 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 3 OF 14 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 2001:497474 BIOSIS
DN PREV200100497474
TI Gene transfer to the nervous system using Equine Infectious Anaemia Virus based lentiviral vectors.
AU Azzouz, M. (1); Martin-Rendon, E. (1); Rohll, J. B. (1); Ellard, F. M. (1); Olsen, A. (1); Carter, E. E. (1); Mitrophanous, K. A. (1); Kingsman, S. M. (1); Mazarakis, N. D. (1)
CS (1) Neurobiology, Oxford Biomedica, Oxford, OX4 4GA UK
SO Society for Neuroscience Abstracts, (2001) Vol. 27, No. 1, pp. 526. print.
Meeting Info.: 31st Annual Meeting of the Society for Neuroscience San Diego, California, USA November 10-15, 2001
ISSN: 0190-5295.
DT Conference
LA English
SL English
AB The potential of a non-primate lentiviral vector based on Equine Infectious Anaemia Virus (EIAV) to transfer the reporter gene LacZ into the **central nervous system** (**CNS**)
was investigated. We have compared the transduction efficiency of EIAV vectors pseudotyped with either vesicular stomatitis virus glycoprotein (VSV-G) or rabies virus glycoprotein (rabies-G). The rabies-G and VSV-G pseudotyped lentiviral vectors can infect approximately 33,000 and 30,000 cells in the striatum, respectively after stereotaxic delivery of 2 mul of the viral solution. VSV-G vectors infect mainly neurons. Rabies-G pseudotyped vectors transduce both neurons and glia but in contrast to VSV-G pseudotyped vectors can be retrogradely transported to neuronal cell bodies that are anatomically linked to the site of injection. The present study demonstrates long-term expression of the reporter gene LacZ in the **CNS** (up to 8 months). We have also adopted a dopamine replacement strategy in animal model of **Parkinson**'s **disease**. We
have therefore generated EIAV tricistronic vector that are able to express the three enzymes involved in dopamine production: tyrosine hydroxylase, **aromatic amino acid** dopa **decarboxylase**
and GTP cyclohydrolase 1. Stereotaxic injection of this vector in the striatum of the 6-OHDA animal model results in gene expression in vivo. This vector system may thus constitute an excellent tool to evaluate potential therapies in animal models of neurodegenerative diseases.

L12 ANSWER 4 OF 14 MEDLINE
AN 2001380603 MEDLINE
DN 21330472 PubMed ID: 11436352
TI Gene therapy for Parkinson's disease: determining the genes necessary for optimal dopamine replacement in rat models.
AU Kang U J; Lee W Y; Chang J W
CS Department of Neurology, University of Chicago, USA.. u-kang@uchicago.edu
NC NS32080 (NINDS)
SO HUMAN CELL, (2001 Mar) 14 (1) 39-48. Ref: 54
Journal code: 8912329. ISSN: 0914-7470.
CY Japan
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200108
ED Entered STN: 20010903
Last Updated on STN: 20010903
Entered Medline: 20010830
AB This article reviews the mechanism of dopamine delivery in the **CNS** in order to determine the optimal set of genes for effective gene therapy in **Parkinson**'s **disease** (PD). Systematic

neurobiological investigation of the biochemical steps has revealed that tyrosine hydroxylase (TH), which has been used in earlier studies, functions only when the essential cofactor, tetrahydrobiopterin (BH1) is present. Transduction of the gene for GTP cyclohydrolase I, the first and rate-limiting step in BH1 synthesis, along with the TH gene, generated cells that are capable of producing L-DOPA spontaneously both in vitro and in vivo. When the **aromatic** L-**amino acid decarboxylase** (**AADC**) gene was added as a third gene, in an attempt to increase the conversion of L-DOPA to dopamine, feedback inhibition by the end product, dopamine, on TH activity resulted. To circumvent this problem, we employed a complementary strategy. Gene transfer of the vesicular monoamine transporter was combined with **AADC** and produced genetically modified cells that can convert L-DOPA to dopamine and store it for gradual release. This approach provided a means to regulate final dopamine delivery by controlling precursor doses and to achieve more sustained delivery of dopamine. Our investigation into determining the genes necessary for optimal dopamine delivery has been facilitated by in vivo biochemical assays using microdialysis. This technique has provided us with a clear and quantitative tool to compare the effects of various genes involved in dopamine synthesis and processing.

L12 ANSWER 5 OF 14 MEDLINE DUPLICATE 1
AN 2000395327 MEDLINE
DN 20341177 PubMed ID: 10877910
TI Convection-enhanced delivery of AAV vector in parkinsonian monkeys; in vivo detection of gene expression and restoration of dopaminergic function using pro-drug approach.
AU Bankiewicz K S; Eberling J L; Kohutnicka M; Jagust W; Pivirotto P; Bringas J; Cunningham J; Budinger T F; Harvey-White J
CS Molecular Therapeutics Section, LMMN, NINDS, Bethesda, Maryland 20892, USA.
SO EXPERIMENTAL NEUROLOGY, (2000 Jul) 164 (1) 2-14.
Journal code: 0370712. ISSN: 0014-4886.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200008
ED Entered STN: 20000824
Last Updated on STN: 20000824
Entered Medline: 20000816
AB Using an approach that combines gene therapy with **aromatic** l-**amino acid decarboxylase** (**AADC**) gene and a pro-drug (l-dopa), dopamine, the neurotransmitter involved in **Parkinson's disease**, can be synthesized and regulated. Striatal neurons infected with the **AADC** gene by an adeno-associated viral vector can convert peripheral l-dopa to dopamine and may therefore provide a buffer for unmetabolized l-dopa. This approach to treating **Parkinson's disease** may reduce the need for l-dopa/carbidopa, thus providing a better clinical response with fewer side effects. In addition, the imbalance in dopamine production between the nigrostriatal and mesolimbic dopaminergic systems can be corrected by using **AADC** gene delivery to the striatum. We have also demonstrated that a fundamental obstacle in the gene therapy approach to the **central nervous system**, i.e., the ability to deliver viral vectors in sufficient quantities to the whole brain, can be overcome by using convection-enhanced delivery. Finally, this study demonstrates that positron emission tomography and the **AADC** tracer, 6-[(18)F]fluoro-l-m-tyrosine, can be used to monitor gene therapy in vivo. Our therapeutic approach has the potential to restore dopamine production, even late in the disease process, at levels that can be maintained during continued nigrostriatal degeneration.

L12 ANSWER 6 OF 14 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 2001:88086 BIOSIS
DN PREV200100088086
TI Human neural stem cells transfected with Nurr1 gene express dopaminergic phenotype.
AU Lee, M. A. (1); Lee, H. S.; Jung, S. H.; Park, S. Y.; Huh, S. O.; Ryu, J. K.; Kim, H. J.; Jin, B. K.; Ichinose, H.; Kim, S. U.
CS (1) Ajou University, Suwon South Korea
SO Society for Neuroscience Abstracts, (2000) Vol. 26, No. 1-2, pp. Abstract No.-313.7. print.
Meeting Info.: 30th Annual Meeting of the Society of Neuroscience New Orleans, LA, USA November 04-09, 2000 Society for Neuroscience . ISSN: 0190-5295.
DT Conference
LA English
SL English
AB Neural stem cells(NSCs) of the **CNS** have recently aroused a great deal of interest not only because of their importance in basic neural development but also their therapeutic potential for neurological **diseases** such as **Parkinson disease** and stroke.
During the **CNS** development, specification of midbrain DA system is determined by two molecular cascades.In one pathway,FGF-8,sonic hedgehog and transcription factor Nurr1 specify DA neurotransmitter phenotype, and in the another, transcription factors Lmx1b and Ptx3 are important. In Nurr1 knock-out mouse, TH positive cells fail to appear in substantia nigra, indicating that Nurr1 is essential in specification of DA phenotype. In this study, we used immortalized human NSCs retrovirally transduced with Nurr1 gene to probe the Nurr1-mediated mechanism to induce DA phenotype. While Nurr1 overexpression alone did not generate DA phenotype in NSCs, application of retinoid and foskolin induced expression of TH and **AADC** mRNAs. In addition, co-cultures of Nurr1 expressing NSCs with human astrocytes induced a marked increase of TH expression. In this co-culture system, addition of retinoids and foskolin dramatically increased expression of TH. These results indicate that the immortalized human NSCs with Nurr1 gene have the clinical utility for cell replacement for patients suffering from **Parkinson disease**(supported by KOSEF)

L12 ANSWER 7 OF 14 CAPLUS COPYRIGHT 2003 ACS
AN 1999:763910 CAPLUS
DN 132:19624
TI Convection-enhanced delivery of AAV vectors to the **CNS** and therapeutic use thereof
IN Bankiewicz, Krys; Cunningham, Janet; Eberling, Jamie L.
PA Avigen, Inc., USA; Lawrence Berkeley National Laboratory
SO PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9961066	A2	19991202	WO 1999-US11687	19990526
	WO 9961066	A3	20000504		
	W: CA, JP				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	CA 2329259	AA	19991202	CA 1999-2329259	19990526
	EP 1080202	A2	20010307	EP 1999-925906	19990526
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	US 6309634	B1	20011030	US 1999-320171	19990526
	JP 2002516295	T2	20020604	JP 2000-550525	19990526

US 2002141980 A1 20021003 US 2001-887854 20010621
PRAI US 1998-86949P P 19980527
US 1999-134748P P 19990518
US 1999-320171 A1 19990526
WO 1999-US11687 W 19990526
AB Methods of delivering viral vectors, particularly recombinant adeno-assocd. virions, to the **CNS** are provided. Also provided are methods of treating Parkinson's Disease.

L12 ANSWER 8 OF 14 MEDLINE DUPLICATE 2
AN 1998268436 MEDLINE
DN 98268436 PubMed ID: 9607420
TI Significant behavioral recovery in Parkinson's disease model by direct intracerebral gene transfer using continuous injection of a plasmid DNA-liposome complex.
AU Imaoka T; Date I; Ohmoto T; Nagatsu T
CS Department of Neurological Surgery, Okayama University Medical School, Japan.
SO HUMAN GENE THERAPY, (1998 May 1) 9 (7) 1093-102.
Journal code: 9008950. ISSN: 1043-0342.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199808
ED Entered STN: 19980817
Last Updated on STN: 20000303
Entered Medline: 19980804
AB As an alternative to virus-mediated gene transfer, we previously demonstrated a simple, safe, and efficient transfer of foreign gene into the **central nervous system** using continuous injection of a plasmid DNA-cationic liposome complex. To explore whether this approach can be applied to the treatment of certain neurological disorders, we used an experimental model of **Parkinson**'s **disease** (PD) in the present study. Following continuous injection for 7 days, tyrosine hydroxylase (TH) and **aromatic** L-**amino acid decarboxylase** (**AADC**) genes carried by a bovine papilloma virus-based plasmid vector were efficiently introduced into glial cells in the striatum of 6-hydroxydopamine-lesioned rats. Significant recovery in apomorphine-induced rotational behavior of PD models was obtained by transfection of TH gene and this effect continued for up to 5 weeks after injection. Moreover, cotransfection of TH with **AADC** genes was readily accomplished by this procedure and resulted in a greater and longer-lasting improvement of apomorphine-induced rotational behavior than was achieved by transfection of TH gene alone. We suggest that this approach is a controllable and manageable alternative to other methods of gene therapy for the treatment of PD.

L12 ANSWER 9 OF 14 MEDLINE DUPLICATE 3
AN 97271203 MEDLINE
DN 97271203 PubMed ID: 9126154
TI L-Dopa and dopamine-producing gene cassettes for gene therapy approaches to Parkinson's disease.
AU Moffat M; Harmon S; Haycock J; O'Malley K L
CS Department of Anatomy and Neurobiology, Washington University School of Medicine, St. Louis, Missouri 63110, USA.
SO EXPERIMENTAL NEUROLOGY, (1997 Mar) 144 (1) 69-73.
Journal code: 0370712. ISSN: 0014-4886.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199705

ED Entered STN: 19970602
Last Updated on STN: 19990129
Entered Medline: 19970520

AB As an aid in the development of vector systems for use in gene therapy paradigms of **central nervous system** disorders such as **Parkinson**'s **disease**, we have developed L-Dopa or dopamine-producing gene cassettes. Specifically, a human tyrosine hydroxylase cDNA (HTH-2) was rendered constitutively active by truncation of the N-terminal regulatory domain (tHTH). In addition, a bicistronic construct capable of directing the production of dopamine was created by inserting an internal ribosome entry site downstream of tHTH followed by the coding sequences of **aromatic amino acid decarboxylase**. All three constructs generated immunoreactive peptides of the predicted size, were enzymatically active, and produced L-Dopa (HTH-2, tHTH) or dopamine (bicistronic construct) following transient transfection of COS-7 cells. These constructs, in conjunction with viral or nonviral expression systems, may be efficacious in gene therapy approaches to **Parkinson**'s **disease**.

L12 ANSWER 10 OF 14 MEDLINE DUPLICATE 4
AN 95379867 MEDLINE
DN 95379867 PubMed ID: 7651438
TI L-dihydroxyphenylalanine and its decarboxylase: new ideas on their neuroregulatory roles.
CM Comment in: Mov Disord. 1996 Jul;11(4):462-3
AU Opacka-Juffry J; Brooks D J
CS MRC Cyclotron Unit, Hammersmith Hospital, London, England.
SO MOVEMENT DISORDERS, (1995 May) 10 (3) 241-9. Ref: 54
Journal code: 8610688. ISSN: 0885-3185.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199509
ED Entered STN: 19951005
Last Updated on STN: 19980206
Entered Medline: 19950928

AB Recent experimental reports concerning L-dihydroxyphenylalanine (L-DOPA) and **aromatic** L-**amino acid decarboxylase** (**AADC**, L-DOPA decarboxylase) are reviewed in this article. Both in vitro and in vivo data now suggest that L-DOPA is an endogenous neuroactive compound that is released from neurons and acts as a neurotransmitter or neuromodulator in the brain. Administration of exogenous L-DOPA affects dopamine receptor status, **AADC** activity, and mitochondrial oxidation in experimental animals. The type and severity of these effects depend on the duration of the treatment. These findings may partly explain the limited efficacy of L-DOPA therapy in **Parkinson**'s **disease** (PD). **AADC** also plays a controlling role in the **central nervous system**, being a regulatory enzyme in the synthesis of a putative neuromodulator 2-phenylethylamine and other trace amines. Recent experimental findings on **AADC** activity and localisation are of importance because they suggest that striatal [18F]DOPA uptake used as an indicator of PD progression in positron emission tomography (PET) studies is likely to overestimate nigrostriatal integrity in advanced PD. Possible new PET tracers of presynaptic dopaminergic function are discussed in this context.

L12 ANSWER 11 OF 14 SCISEARCH COPYRIGHT 2003 ISI (R)
AN 96:555260 SCISEARCH
GA The Genuine Article (R) Number: BF87C
TI **AROMATIC L-AMINO-ACID DECARBOXYLASE**

MODULATION AND **PARKINSONS-DISEASE**
AU NEFF N H (Reprint); HADJICONSTANTINOU M
CS OHIO STATE UNIV, COLL MED, DEPT PHARMACOL, COLUMBUS, OH, 43210 (Reprint); OHIO STATE UNIV, COLL MED, DEPT PSYCHIAT, COLUMBUS, OH, 43210
CYA USA
SO PROGRESS IN BRAIN RESEARCH, (1995) Vol. 106, pp. 91-97. ISSN: 0079-6123.
DT General Review; Journal
LA ENGLISH
REC Reference Count: 44

L12 ANSWER 12 OF 14 MEDLINE DUPLICATE 5
AN 93297020 MEDLINE
DN 93297020 PubMed ID: 8100096
TI Is L-dopa an endogenous neurotransmitter?.
AU Misu Y; Goshima Y
CS Department of Pharmacology, Yokohama City University School of Medicine, Kanagawa Prefecture, Japan.
SO TRENDS IN PHARMACOLOGICAL SCIENCES, (1993 Apr) 14 (4) 119-23. Ref: 31 Journal code: 7906158. ISSN: 0165-6147.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199307
ED Entered STN: 19930806
Last Updated on STN: 19950206
Entered Medline: 19930719
AB Since the 1960s, L-3,4-dihydroxyphenylalanine (L-dopa), a precursor of dopamine, has been thought to occur in the cytoplasm of catecholaminergic neurones. L-Dopa is traditionally believed to be an inert amino acid that exerts actions and effectiveness in **Parkinson's disease** via its conversion to dopamine by L-**aromatic amino acid decarboxylase**. In contrast to this generally accepted idea, Yoshimi Misu and Yoshio Goshima propose, in this Viewpoint article, that L-dopa itself is an endogenous neurotransmitter or neuromodulator in the **CNS**. This hypothesis is mainly based on the findings that L-dopa is released in a transmitter-like manner and that exogenously applied levodopa produces some responses.

L12 ANSWER 13 OF 14 MEDLINE DUPLICATE 6
AN 88050207 MEDLINE
DN 88050207 PubMed ID: 3314916
TI A mouse model of N-methyl-4-phenyl-1,2,3,6-tetrahydropyridine induced parkinsonism: effect of norepinephrine terminal destruction.
AU Nishi K; Kondo T; Narabayashi H
CS Department of Neurology, Juntendo University School of Medicine, Tokyo, Japan.
SO NO TO SHINKEI. BRAIN AND NERVE, (1987 Jul) 39 (7) 663-72. Ref: 34 Journal code: 0413550. ISSN: 0006-8969.
CY Japan
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW LITERATURE)
LA Japanese
FS Priority Journals
EM 198712
ED Entered STN: 19900305
Last Updated on STN: 20000303
Entered Medline: 19871229
AB N-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) has been reported to cause chronic Parkinsonism in humans, primates, and long lasting striatal

dopamine depletion in mice. Acute animal models thus produced closely resemble **Parkinson's disease**. There are, however, two major differences. The one is a lack of Lewy bodies and the other is that norepinephrine system is relatively well preserved in the model. So the acute animal model is better considered a nigrostriatal dopamine deficiency model. We have produced another model by adding N-2-chloroethyl-N-ethyl-2-bromobenzyl-amine (DSP4) to MPTP. This material is known to produce selective destruction of norepinephrine terminal in the **central nervous system** as well as in the periphery. Both norepinephrine system and dopamine system are severely depressed in this model, and the functional role of norepinephrine system was investigated by comparing two models. 90 male C57 black mice weighing 20-25 grams were used. MPTP (Aldrich) was dissolved in sterile distilled water with 5% ethanol solution. Experimental animals were divided into three groups. i) control group; in this group animals received vehicles alone. ii) MPTP group; in this group, mice received daily i.p. doses of MPTP 30 mg/kg for consecutive 10 days, thus total doses of MPTP was 300 mg/kg. iii) MPTP & DSP4 group; in this group animals received daily i.p. doses of MPTP 30 mg/kg for consecutive 10 days and at the last day of MPTP injection they received DSP4 50 mg/kg i.p.. 7 to 14 days after the last injection of MPTP both treated and control mice received an intraperitoneal injection of L-DOPA (200 mg/kg & **aromatic** L-**amino acid decarboxylase** mg/kg) and the effect of this drug on three groups were investigated by using behavioral, biochemical and histofluorescence method. Histofluorescence studies by GA-FAS method revealed severe reduction of nigrostriatal dopamine in MPTP treated mice. Mesolimbic and mesocortical dopamine systems seemed relatively preserved. There was no apparent changes in locus coeruleus norepinephrine system. In MPTP & DSP4 treated mice marked reduction of norepinephrine terminal fluorescence as well as nigrostriatal dopamine system was observed. Chemical analysis of norepinephrine and dopamine by HPLC confirmed histofluorescence studies. Behavioral studies were analyzed by Automex locomotor activity meter. Marked increase of locomotor activity was observed in MPTP treated mice after L-DOPA administration.(ABSTRACT TRUNCATED AT 400 WORDS)

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TI PLASMA ACCUMULATION AND METABOLISM OF ORALLY ADMINISTERED SINGLE DOSE L-5 HYDROXY TRYPTOPHAN IN MAN.
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AB One current approach to the investigation of the neuro- and psychotropic effects of enhancing serotoninergic neurotransmission in the **central nervous system** of man is administration of L-5-hydroxytryptophan (5-HTP). Single oral doses of (5-HTP) were administered in combination with L-aromatic amino acid decarboxylase inhibitors. The time courses of plasma concentrations of 5-HTP, 5-hydroxytryptamine (5-HT) and 5-hydroxyindoleacetic acid (5-HIAA) and the concentrations of 5-HT in blood platelets were measured. Carbidopa enhanced the rise in plasma concentrations of 5-HTP 5- to 15-fold and counteracted the increase in plasma 5-HIAA levels induced by 5-HTP alone. A single dose of the decarboxylase inhibitor was equipotent to 14 days' pretreatment. Plasma or platelet concentrations of 5-HT failed to reflect the metabolism of 5-HTP. The ratio of 5-HTP to carbidopa influenced the systemic bioavailability of single dose administered 5-HTP, indicating dose dependent absorption kinetics. Co-administration of L-dopa with 5-HTP and decarboxylase inhibitors had no effect on gastrointestinal absorption of 5-HTP in 6 parkinsonian patients.